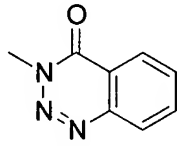
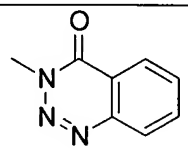
CN		rac	or
OCF_3		rac	.

6. (Amended)A pharmaceutical composition which as active constituent contains at least one compound according to claim 5 mixed together with at least one pharmaceutically tolerable essentially non-toxic vehicle or excipient.

7. (Amended) A process for the preparation of a pharmaceutical composition according to claim 6 , comprising formulating a compound of claim 5 with at least one pharmaceutically tolerable essentially non-toxic vehicle or excipient.

Remarks / Explanations

As a result of this preliminary amendment, claims 1-8 are pending in the application. No new matter has been added.

Claims 1-7 have been amended to bring them into a form more in keeping with standard US practice.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

In view of the above amendments and explanations, this application is deemed to be in condition for allowance, and allowance is accordingly requested.

Respectfully submitted,

Reg. No. 31018
Phone: (203) 812-2712
Date: _____

William F. Gray
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400 Morgan Lane
West Haven, CT 06516-4175

Version with markings to show changes made:

In the claims:

Claims 1-7 have been amended as shown below:

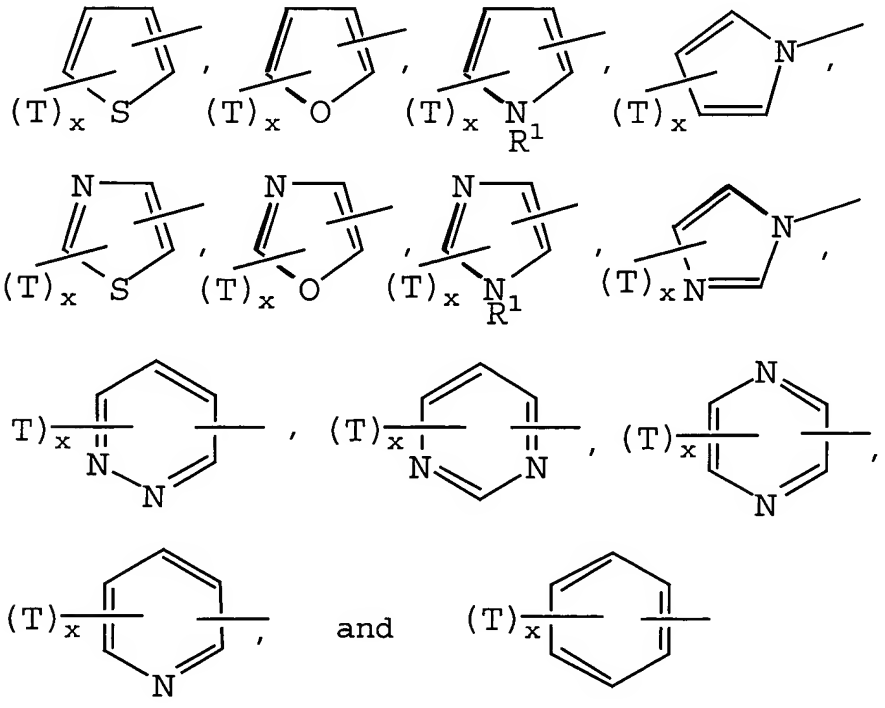
Unamended claim 8 is shown in the list below for the convenience of the examiner.

1. (Amended)[Use of the compounds] A method for the treatment or prophylaxis of multiple sclerosis, comprising administering to a mammal an effective amount of a compound of the generalized formula (I):

$$(T)_XA\text{-}B\text{-}D\text{-}E\text{-}CO_2H \qquad (I)$$

wherein

(a) $(T)_XA$ represents a substituted or unsubstituted aromatic or heteroaromatic moiety selected from the group consisting of:



wherein R^1 represents H or alkyl of 1 - 3 carbons; and

each T represents a substituent group, independently selected from the group consisting of:

* the halogens -F, -Cl, -Br, and -I;
* alkyl of 1 - 10 carbons;
* haloalkyl of 1 - 10 carbons;
* haloalkoxy of 1-10 carbons;
* alkenyl of 2 - 10 carbons;
* alkynyl of 2 - 10 carbons;
* $-(CH_2)_pQ$, wherein
  p is 0 or an integer 1 - 4,
* -alkenyl-Q, wherein
  said alkenyl moiety comprises 2 - 4 carbons; and
* -alkynyl-Q, wherein
  said alkynyl moeity comprises 2-7 carbons; and

Q is selected from the group consisting of aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, -CN, -CHO, $-NO_2$, $-CO_2R^2$, $-OCOR^2$, $-SOR^3$, $-SO_2R^3$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-C(O)R^2$, $-N(R^4)_2$, $-N(R^2)COR^2$, $-N(R^2)CO_2R^3$, $-N(R^2)CON(R^4)_2$, $-CHN_4$, $-OR^4$, and $-SR^4$;

wherein

R^2 represents H;
alkyl of 1 - 6 carbons;
aryl of 6 - 10 carbons;
heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or
arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R^3 represents alkyl of 1 - 4 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R^4 represents H;

alkyl of 1 - 12 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons;

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

alkenyl of 2 - 12 carbons;

alkynyl of 2 - 12 carbons;

$-(C_qH_{2q}O)_rR^5$ wherein q is 1-3; r is 1 - 3; and R^5 is H provided q is greater than 1, or alkyl of 1 - 4 carbons, or phenyl;

alkylenethio terminated with H, alkyl of 1-4 carbons, or phenyl;

alkyleneamino terminated with H, alkyl of 1-4 carbons, or phenyl]

$-(CH_2)_sX$ wherein s is 1 - 3 and X is halogen;

$-C(O)OR^2$; or

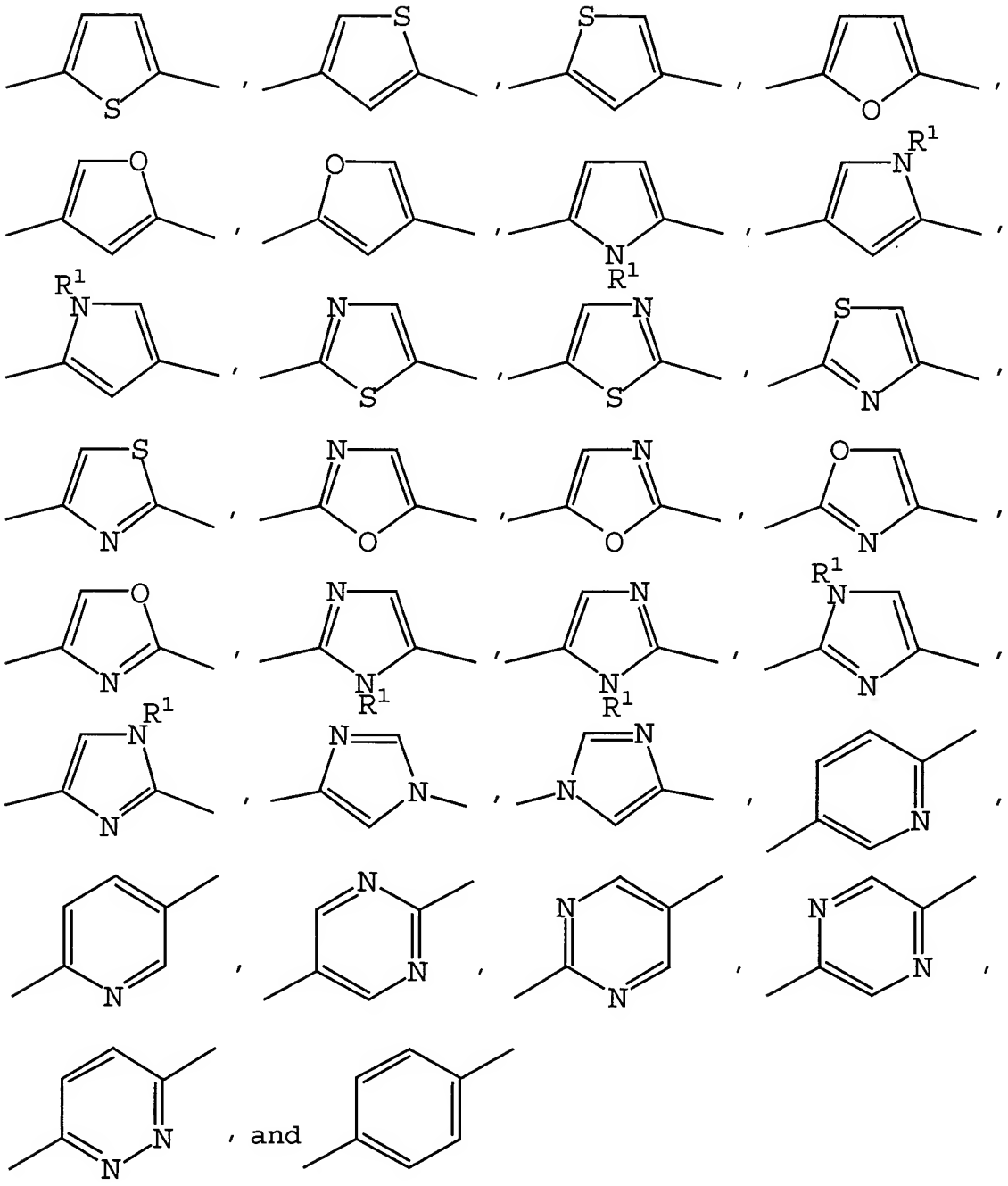
$-C(O)R^2$;

and with the provisos that a) when two R^4 groups are situated on a nitrogen, they may be joined by a bond to form a heterocycle, and b)

unsaturation in a moiety which is attached to Q or which is part of Q is separated from any N, O, or S of Q by at least one carbon atom, and

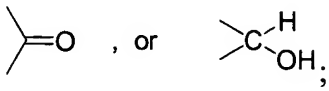
x is 0, 1, or 2;

(b) B represents a bond or an optionally substituted aromatic or heteroaromatic ring containing 0-2 substituents T, which substitutents T may independently have the meaning specified under (a), the B rings being selected from the group consisting of:



wherein R^1 is as defined above; and each R^1 may be the same or different:

(c) D represents



(d) E represents a chain of n carbon atoms bearing m substituents R^6, wherein said R^6 groups are independent substituents, or constitute spiro or nonspiro rings in which a) two groups R^6 are joined, and taken together with the chain atom(s) to which said two R^6 group(s) are attached, and any intervening chain atoms, constitute a 3 - 7 membered ring, or b) one group R^6 is joined to the chain on which said one group R^6 resides, and taken together with the chain atom(s) to which said R^6 group is attached, and any intervening chain atoms, constitutes a 3 - 7 membered ring; and wherein

n is 2 or 3;

m is an integer of 1 - 3;

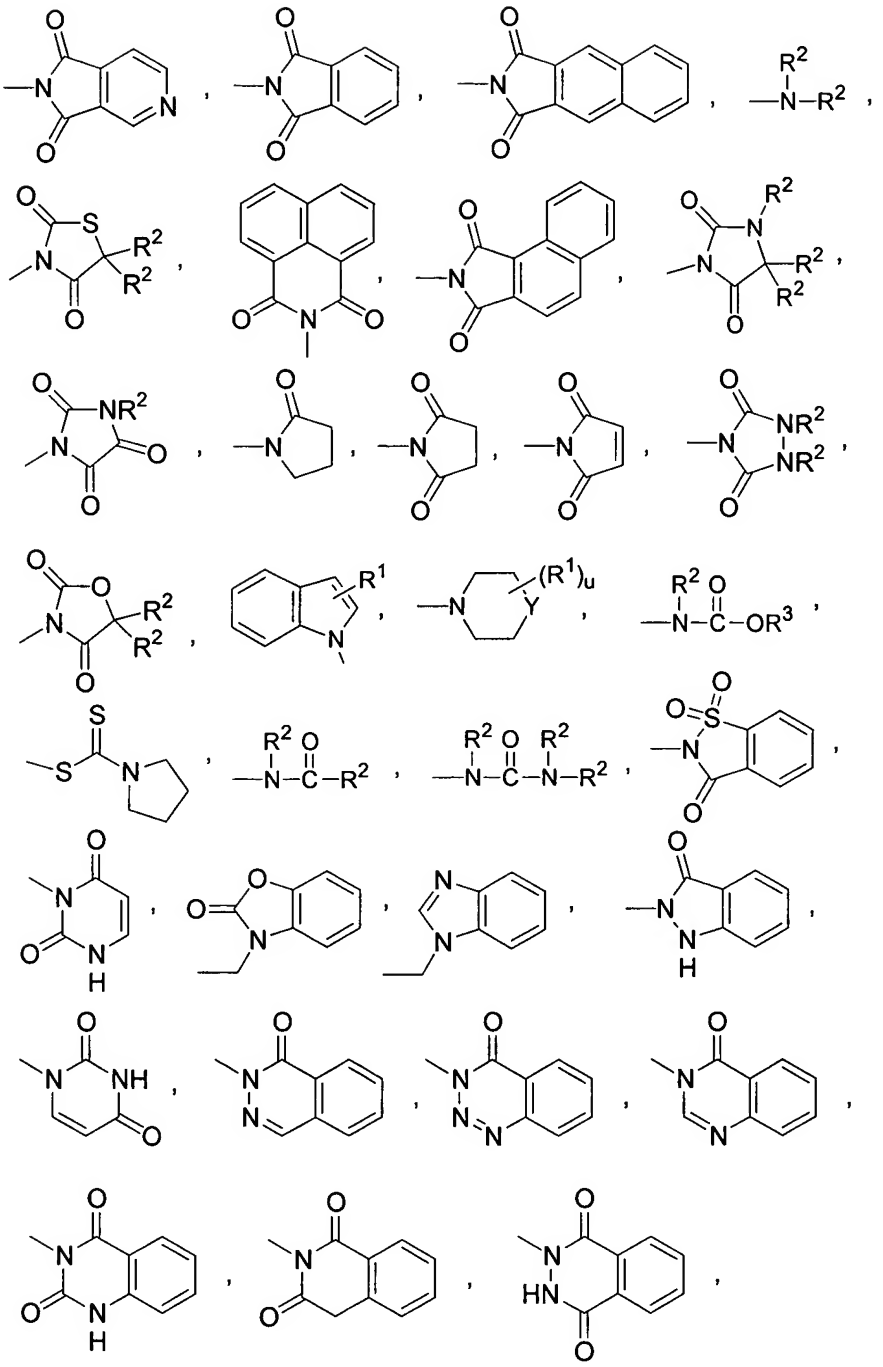
each group R^6 is independently selected from the group consisting of:

* fluorine;
* hydroxyl, with the proviso that a single carbon may bear no more than one hydroxyl substituent;
* alkyl of 1 - 10 carbons;
* aryl of 6 - 10 carbons;
* heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;
* arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;
* heteroaryl-alkyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 8 carbons;
* alkenyl of 2 - 10 carbons;
* aryl-alkenyl wherein the aryl portion contains 6 - 10 carbons and the alkenyl portion contains 2 - 5 carbons;
* heteroaryl-alkenyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkenyl portion contains 2 - 5 carbons;
* alkynyl of 2 - 10 carbons;

* aryl-alkynyl wherein the aryl portion contains 6 - 10 carbons and the alkynyl portion contains 2 - 5 carbons;
* heteroaryl-alkynyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkynyl portion contains 2 - 5 carbons;
* $-(CH_2)_tR^7$ wherein

  t is 0 or an integer of 1 - 5; and

  R^7 is selected from the group consisting of



and corresponding heteroaryl moieties in which the aryl portion of an aryl-containing R^7 group comprises 4 - 9 carbons and at least one N, O, or S heteroatom;

wherein

Y represents O or S;

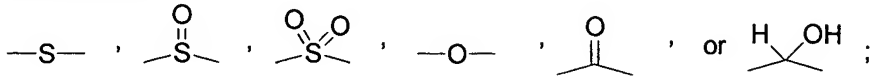
R^1, R^2, and R^3 are as defined above; and each R^1, R^2 or R^3 may be the same or different; and

u is 0, 1, or 2; and

* $-(CH_2)_vZR^8$ wherein

v is 0 or an integer of 1 to 4; and

Z represents



;

R^8 is selected from the group consisting of:

alkyl of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion contains 6 to 10 carbons and the alkyl portion contains 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$-C(O)R^9$ wherein R^9 represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion contains 6 - 10 carbons or is heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 4 carbons;

and with the provisos that

- when R^8 is $-C(O)R^9$, Z is S or O;
- when Z is O, R^8 may also be $-(C_qH_{2q}O)_rR^5$ wherein q, r, and R^5 are as defined above; and

* $-(CH_2)_wSiR^{10}{}_3$ wherein

w is an integer of 1 to 3; and

R^{10} represents alkyl of 1 to 2 carbons;

and with the proviso that

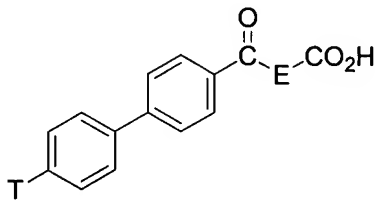
- aryl or heteroaryl portions of any of said T or R^6 groups optionally may bear up to two substituents selected from the group consisting of $-(CH_2)_yC(R^4)(R^3)OH$, $-(CH_2)_yOR^4$, $-(CH_2)_ySR^4$, $-(CH_2)_yS(O)R^4$, $-(CH_2)_yS(O)_2R^4$, $-(CH_2)_ySO_2N(R^4)_2$, $-(CH_2)_yN(R^4)_2$, $-(CH_2)yN(R^4)COR^3$, $-OC(R^4)_2O-$ in which both oxygen atoms are connected to the aryl ring, $-(CH_2)_yCOR^4$, $-(CH_2)_yCON(R^4)_2$, $-(CH_2)_yCO_2R^4$, $-(CH_2)_yOCOR^4$, -halogen, $-CHO$, $-CF_3$, $-NO_2$, -CN, and R^3 wherein

y is 0 - 4; and

R^3 and R^4 are as defined above, and each R^3 and R^4 may be the same or different; and any two R^4 which are attached to one nitrogen may be joined to form a heterocycle;

[and] or a pharmaceutically acceptable salt[s and] or prodrug[s] thereof [for the manufacturing of drugs for the treatment and prevention of multiple sclerosis].

2. (Amended)[Use] The method according to claim 1 wherein the method comprises administering [of] a compound[s] of the general formula (I')



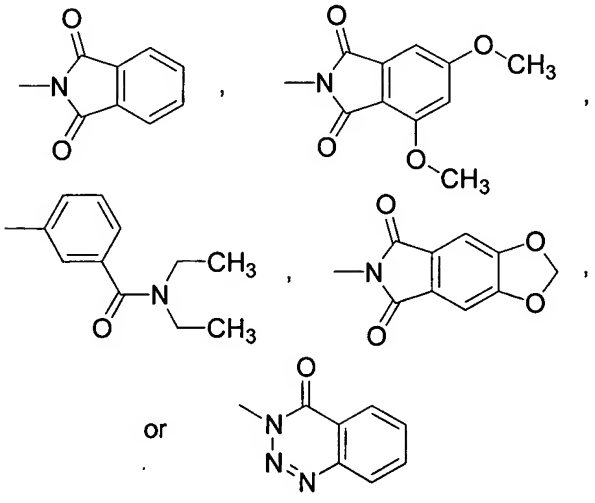
(I')

wherein

T is (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy, chloride, bromide, fluoride, acetoxy, hydroxy, cyano, trifluoromethyl or trifluoromethoxy,

CO-E-CO_2H represents a 3-carboxyl-5-(R^7)-pentan-1-on-1-yl- or a [2-carboxyl-3-(R^7)-methyl-cyclopentan-1-yl]-carbonyl-residue, wherein

R^7 represents a group of the formula



[and their salts] or a salt thereof.

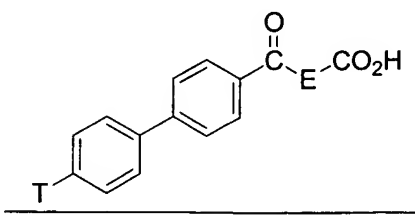
3. (Amended)[Use] The method according to claim 2, characterized in that [the] one emantiomer of a pair of emantiomers at a chiral center adjacent to the carboxylic acid moiety of the group of the formula CO-E-CO_2H in compounds of the general formula (1') more potently inhibits MMP-2 and/or MMP-9.

4. (Amended)[Use] The method according to claim 1, wherein the compound is selected from the group consisting of

(+)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-(4'-ethoxyl[1,1'-biphenyl]-4-yl)-4-oxobutanoic acid,
(+)-4-(4'-chloro[1,1'-biphenyl]-4-yl)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-oxobutanoic acid,

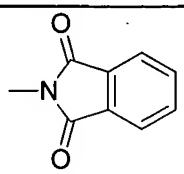
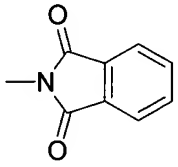
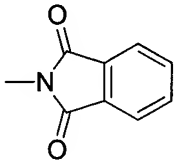
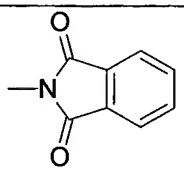
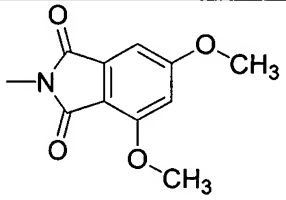
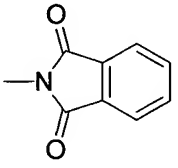
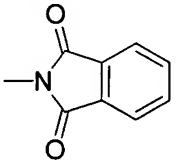
[or a salt] and salts thereof.

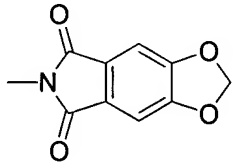
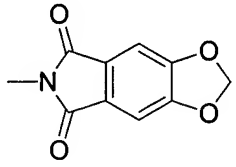
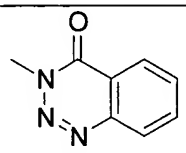
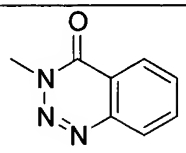
5. (Amended) [Compounds] A compound of the general formula (I'),



(I')

wherein CO-E-CO_2H represents a 3-carboxyl-5-R^7-pentan-1-on-1-yl- residue, and wherein T and R^7 have the meaning indicated in the following table:

T	**R^7**	**racemate, (+)- or (-)-enantiomer**	
OEt		(+)	;
OEt		(-)	;
OAc		rac	;
OH		rac	;
Cl		rac	;
Br		(+)	;
Br		(-)	;

Cl		(+)	;
Cl		(-)	;
CN		rac	or
OCF_3		rac	.

6. (Amended)[Pharmaceutical] A pharmaceutical composition which as active constituent contains at least one compound according to claim 5 mixed together with at least one pharmaceutically tolerable essentially non-toxic vehicle or excipient.

7. (Amended) [Process] A process for the preparation of a pharmaceutical composition according to claim 6 , comprising formulating a compound of claim 5 with at least one pharmaceutically tolerable essentially non-toxic vehicle or excipient.

8. Compound according to claim 5 for use as a medicament in the treatment of humans or animals.